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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,084	08/20/2003	Yoshimi Takai	2144.0100000/RWE/ALS	4948

26111 7590 04/19/2007
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER

BASI, NIRMAL SINGH

ART UNIT	PAPER NUMBER
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1646

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/644,084

Applicant(s)

TAKAI ET AL.

Examiner

Nirmal S. Basi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 and 19-23 is/are pending in the application.
- 4a) Of the above claim(s) 2,7-13 and 19-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-6,14,15 and 23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 December 2006 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- 1) ☒ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 10/6/05.

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

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DETAILED ACTION

1. Amendment filed 1/24/07 has been entered. Applicant has amended claims 1, 4, 6, and added new claim 23. Claims 1 3-6, 14-15 and 23 are being examined as being directed to the elected invention. Claims 2, 7-13, 16-22 are either withdrawn or cancelled. Examiner rejections are recast below to address the amended claims. Applicants arguments have been fully considered but are not deemed persuasive to overcome the rejection of the amended claims as discussed below.

2. IDS filed 10/6/05 was considered on 8/15/06 but references AS22, AT22 and AR23 were not initialed. This was an oversight by the Examiner and references AS22, AT22 and AR23 have now been initialed as being considered and are attached with this Office action. References AR9, AR19 have been initialed again just to remove any ambiguity as to if they were considered or not.

3. The drawings remain objected to because Figure 2B is too dark and the figure is not legible. Applicants have filed new drawing on 12/22/06. Figure 2B is completely black and shows no data. Appropriate correction is required.

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application for the reasons given above. Applicant is advised to employ the services of a competent patent draftsman outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

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4. a) The amendment filed 12/28/06 is objected to because it does not include the statement "the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing" and, where applicable, includes no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b) or 1.825(d). A statement that the sequence listing information is identical is required. Further to replace the existing sequence with that filed 12/28/06 a statement to that effect is required.
- b) A partial copy of the sequence listing on the CRF is attached. The CRF contained errors which were corrected by STIC, see attached "RAW SEQUENCE LISTING" (Appendix 1).

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 3 -6, 14-15 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim is indefinite because of the use of the phrase "nucleotide sequence corresponding to". It is suggested to overcome the rejection Applicants amend the claim to "nucleotide sequence set forth at". Further, claim I is indefinite because it is not clear how the polynucleotide binds afadin or actinin. It is suggested to overcome the rejections the claim be amended as follows:

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1. An isolated and purified polynucleotide selected from the group consisting of:

(a) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO: 2;

(b) a polynucleotide comprising the nucleotide sequence set forth at ~~of corresponding to~~ position 80 to 1924 in SEQ ID NO:1; and

(c) a polynucleotide comprising the nucleotide sequence with at least 95% homology to the nucleotide sequence set forth at ~~corresponding to~~ position 80 to 1924 in SEQ ID NO: 1, wherein the polynucleotide encodes a polypeptide which binds ~~which have the binding activity to~~ afadin and/or actinin.

Claim 6 is rejected because it is broader in scope than the base claim from which it depends.

Claims 3 -5, 14-15 and 23 are rejected for depending on an indefinite base claim and fail to resolve the issued raised above.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim is drawn to:

An isolated and purified polynucleotide, which comprises at least 15

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nucleotides of claim 1.

The claims, as written, encompass polynucleotides, which vary substantially in length and also in nucleotide composition. The instant disclosure does not adequately describe the scope of the claimed genus, which has insufficient structural limitations to correspond to the functional limitations. The claims encompass a substantial variety of subgenera including derivatives, allelic variants, chimeric constructs, fusion constructs etc. which may not even contain the critical structural feature of the invention contained in the afadin, actinin α or actinin β binding domain of ADIP.

The specification discloses a polynucleotide (SEQ ID NO:1) encoding a polypeptide (SEQ ID NO:2) which binds afadin, α -actinin-1 or α -actinin-2, wherein the polypeptide comprises the afadin, actinin α or actinin β binding domain disclosed in Figure 3A. The specification also discloses truncated polynucleotide of SEQ ID NO:1 encoding truncated polypeptide SEQ ID NO:2 which binds afadin, α -actinin-1 or α -actinin-2, wherein the polynucleotide comprises the afadin, actinin α or actinin β binding domain disclosed in Figure 3A. The specification is enabled for polynucleotide encoding polypeptide which bind afadin, α -actinin-1 or α -actinin-2, wherein the polypeptide comprises the afadin, actinin α or actinin β binding domain disclosed in Figure 3A.

The critical feature of the invention as it relates structure to function is the afadin, actinin α or actinin β binding domain disclosed in Figure 3A. The structure is the domain contained in the polypeptide of SEQ ID NO:1, and the function is that said domain binds afadin, actinin α or actinin β . The structure has to be a

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minimum length and composition. The critical feature of the invention as it relates to structure and function is not contained, for example, in a polynucleotide that is 15 nucleotides long as claimed in claim 6.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. As cited above many polynucleotide constructs, which combine specific structure to function, are enabled by the disclosure, the claims that do not, as indicated above, are not enabled.

Pertaining to the claim 6 there is no identification of any particular portion of the structure of the peptide of SEQ ID NO:2 that must be conserved for activity. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. The structural limitations in the claim are insufficient to define the genus claimed, which encompasses unrelated peptides.

Naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. When one is unable to envision the detailed constitution of a complex chemical compound having a particular function, such as a peptide or nucleic acid, so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has

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occurred, i.e., until after the peptide or nucleic acid has been isolated. Thus, claiming all peptides or DNAs that achieve a result without defining what means will do so is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. The claims recite a broad arbitrary structural relationship between the claimed polynucleotide sequence and the disclosed polynucleotide of SEQ ID NO:1. Therefore, unrelated peptides to SEQ ID NO:2 are encompassed by the claims.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of peptide, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF'S were

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found to be unpatentable due to lack of written description for that broad class.

The specification provided only the bovine sequence.

Therefore, only isolated polynucleotide of SEQ ID NO:1 encoding the amino acid sequence set forth in SEQ ID NO:2 but not the full breadth of the claims meets the written description provision of 35 U.S.C.112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1 115).

7. Claim 1, and dependent claims 3-6, 15 and 23 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The added material which is not supported by the original disclosure is as follows: A) An isolated and purified polynucleotide comprising the nucleotide sequence corresponding to **position 80 to 1924 in SEQ ID NO: 1**. B) An isolated and purified polynucleotide comprising the nucleotide sequence with **at least 95% homology** to the nucleotide sequence corresponding to **position 80 to 1924 in SEQ ID NO: 1** which have the binding activity to afadin and/or actinin

There is no support in the specification for the species of polynucleotide comprising the nucleotide sequence corresponding to **position 80 to 1924 in**

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SEQ ID NO: 1. There is no support in the specification for the species of polynucleotide comprising the nucleotide sequence with **at least 95% homology** to the nucleotide sequence corresponding to **position 80 to 1924 in SEQ ID NO: 1** which have the binding activity to afadin and/or actinin.

Applicant is required to cancel the new matter in the reply to this Office Action or show support for such a construct.

8. Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The added material which is not supported by the original disclosure is as follows: A)

"An isolated and purified host cell **transformed** with the polynucleotide of claim 1". There is no support in the specification for the host cell **transformed** with the polynucleotide of claim 1.

Applicant is required to cancel the new matter in the reply to this Office Action or show support for such a construct.

9 If applicant overcomes the written description rejection above then claims 1, 3-6, 15 and 23 will be rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated and purified polynucleotide selected from the group consisting of: (a) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO: 2; (b) a polynucleotide

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comprising the nucleotide sequence set forth at position 80 to 1924 in SEQ ID NO:1; and (c) a polynucleotide comprising the nucleotide sequence with at least 95% homology to the nucleotide sequence set forth at position 80 to 1924 in SEQ ID NO: 1, wherein the polynucleotide encodes a polypeptide which binds afadin and/or actinin;, vector comprising said polynucleotide, isolated host cell comprising said vector, method of using said cell to produce the enabled polypeptide of claim 1; and polynucleotide fragments of the polynucleotide of SEQ ID NO:1 which are of sufficient length to be used as specific hybridization probes to detect the polynucleotide encoding the polypeptide which binds afadin, actinin α or actinin β , wherein the polypeptide comprises the afadin, α -actinin-1 or α -actinin-2 binding domain disclosed in Figure 3C, does not reasonably provide enablement for other polynucleotides. The, specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Based on the disclosure a person of ordinary skill in the art would, in light of the specification, be able to isolate polynucleotide encoding a polypeptide which binds afadin, α -actinin-1 or α -actinin-2, comprising the afadin, α -actinin-1 or α -actinin-2 binding domain disclosed in Figure 3C. A person of ordinary skill in the art, in light of the specification, would also be able to produce vector comprising the enabled polynucleotide and host cell comprising said vector and use said host cell to produce the enabled polynucleotide of claim 1.

The scope of the claims, which encompass other polynucleotides

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encoding polypeptides not comprising the afadin, actinin α or actinin β binding domain disclosed in Figure 3C are not enabled by the disclosure. Further the scope of the claims, which encompass other polynucleotides encoding polypeptides comprising the afadin or actinin binding activity but structurally unrelated to the polynucleotide of SEQ ID NO:1 are not enabled by the disclosure. The specification, Figure 3A, discloses the critical structural regions of the polypeptide of SEQ ID NO:2 (ADIP) which is required for afadin, α -actinin-1 or α -actinin-2 binding. ADIP has been shown to bind afadin, α -actinin-1 or α -actinin-2. The claims encompass variant polynucleotides which may have as little as 15 nucleotides in common with the polynucleotide of SEQ ID NO:1 and none of the afadin, α -actinin-1 or α -actinin-2 binding. Applicant has not disclosed how to use said variants. Variant molecules which are structurally unrelated to ADIP are encompassed by the claims. Although these molecules may bind afadin, actinin they may have physiological functions unrelated to the ADIP of instant invention. Applicant has not disclosed how to use said variant molecules. For example, Applicant has not shown how to use variant polynucleotides comprising 15 nucleotides that hybridize to the polynucleotide of SEQ ID NO:1. Said variant polynucleotides comprising 15 nucleotides may be not even contain the critical feature of the invention as it relates structure to function.

Clearly, a single disclosed sequence does not support claims to any polynucleotide comprising 15 nucleotides of SEQ ID NO:1. Due to the large quantity of experimentation necessary to make and use the variant

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polynucleotides of claimed invention lacking with the critical feature of the invention as it relates structure to function, the lack of direction/guidance presented in the specification regarding the identification, purification, isolation and characterization of said variant polynucleotides, the unpredictability of the effects of mutation on the structure and function of variant polynucleotides (since mutations of SEQ ID NO:1 and 2 are also encompassed by the claim), and the breadth of the claim which fail to recite meaningful structural and functional limitations, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope.

10 The rejections of record under 35 U.S.C. 112, first paragraph are maintained for reasons of record as they apply to the amended claims. Claims 1, 3-6, 15-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide encoding a polypeptide which binds afadin, α -actinin-1 or α -actinin-2, wherein the polypeptide comprises the afadin, actinin α or actinin β binding domain disclosed in Figure 3A, vector comprising said polynucleotide, isolated host cell comprising said vector, method of using said cell to produce the enabled polypeptide of claim 1; and polynucleotide fragments of the polynucleotide of SEQ ID NO:1 which are of sufficient length to be used as specific hybridization probes to detect the polynucleotide encoding the polypeptide which binds afadin, actinin α or actinin β , wherein the polypeptide comprises the afadin, α -actinin-1 or α -actinin-2 binding domain disclosed in Figure 3C, does not reasonably provide enablement

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for other polynucleotides. The, specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Based on the disclosure a person of ordinary skill in the art would, in light of the specification, be able to isolate polynucleotide encoding a polypeptide which binds afadin, α -actinin-1 or α -actinin-2, comprising the afadin, α -actinin-1 or α -actinin-2 binding domain disclosed in Figure 3C. A person of ordinary skill in the art, in light of the specification, would also be able to produce vector comprising the enabled polynucleotide and host cell comprising said vector and use said host cell to produce the enabled polynucleotide of claim 1. The rejection is the same as disclosed in the prior office Action.

Prior Art Rejections

Applicants argue the prior art references do not disclose the nucleotide sequence with at least 95% homology to the nucleotide sequence corresponding to position 80-1924 in SEQ ID NO:1. Applicant's arguments have been fully considered but they are not found persuasive. The following rejections are maintained. As seen by the sequence comparisons the polynucleotide sequence shown have at least 95% homology to the nucleotide sequence corresponding to position 80-1924 in SEQ ID NO:1..

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1,3, 4, 6, 15-18 are rejected under 35 U.S.C. 102(b) as being anticipated by The RIKEN Genome Exploration Research group Phase II Team and the FANTOM Consortium (Nature, Vol. 409, pages 563-690, February 8, 2001)

The RIKEN Genome Exploration Research group Phase II Team and the FANTOM Consortium (Nature article, also see attached sequence comparison) disclose a polynucleotide, which has 99.4% query match and 99.9% identity to the polynucleotide of SEQ ID NO:1. Also disclosed are vector comprising said polynucleotide and cell comprising said vector. The disclosed polynucleotide encodes a polypeptide that inherently binds afadin and/or actinin, absent evidence to the contrary.

Therefore the disclosure of the RIKEN Genome Exploration Research group Phase II Team and the FANTOM Consortium meets the limitations of claims 1,3, 4, 6, 15-18, absent evidence to the contrary.

RESULT 1

AK043865

LOCUS AK043865 3185 bp mRNA linear HTC 02-SEP-2005

DEFINITION Mus musculus 10 days neonate cortex cDNA, RIKEN full-length enriched library, clone:A830043F14 product:HYPOTHETICAL 71.0 KDA

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PROTEIN homolog [Mus musculus], full insert sequence.

ACCESSION AK043865

VERSION AK043865.1 GI:26335971

KEYWORDS HTC; CAP trapper.

SOURCE Mus musculus (house mouse)

ORGANISM Mus musculus

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Sciurognathi; Muroidea; Muridae; Murinae; Mus.

REFERENCE 1

AUTHORS Carninci, P. and Hayashizaki, Y.

TITLE High-efficiency full-length cDNA cloning

JOURNAL Meth. Enzymol. 303, 19-44 (1999)

PUBMED 10349636

REFERENCE 2

AUTHORS Carninci, P., Shibata, Y., Hayatsu, N., Sugahara, Y., Shibata, K., Itoh, M., Konno, H., Okazaki, Y., Muramatsu, M. and Hayashizaki, Y.

TITLE Normalization and subtraction of cap-trapper-selected cDNAs to prepare full-length cDNA libraries for rapid discovery of new genes

JOURNAL Genome Res. 10 (10), 1617-1630 (2000)

PUBMED 11042159

REFERENCE 3

AUTHORS Shibata, K., Itoh, M., Aizawa, K., Nagaoka, S., Sasaki, N., Carninci, P., Konno, H., Akiyama, J., Nishi, K., Kitsunai, T., Tashiro, H., Itoh, M., Sumi, N., Ishii, Y., Nakamura, S., Hazama, M., Nishine, T., Harada, A., Yamamoto, R., Matsumoto, H., Sakaguchi, S., Ikegami, T., Kashiwagi, K., Fujiwaka, S., Inoue, K., Togawa, Y., Izawa, M., Ohara, E., Watahiki, M., Yoneda, Y., Ishikawa, T., Ozawa, K., Tanaka, T., Matsuura, S., Kawai, J., Okazaki, Y., Muramatsu, M., Inoue, Y., Kira, A. and Hayashizaki, Y.

TITLE RIKEN integrated sequence analysis (RISA) system--384-format sequencing pipeline with 384 multicapillary sequencer

JOURNAL Genome Res. 10 (11), 1757-1771 (2000)

PUBMED 11076861

REFERENCE 4

AUTHORS The RIKEN Genome Exploration Research Group Phase II Team and the FANTOM Consortium.

TITLE Functional annotation of a full-length mouse cDNA collection

JOURNAL Nature 409, 685-690 (2001)

REFERENCE 5

AUTHORS The FANTOM Consortium, the RIKEN Genome Exploration Research Group Phase I and II Team.

TITLE Analysis of the mouse transcriptome based on functional annotation of 60,770 full-length cDNAs

JOURNAL Nature 420, 563-573 (2002)

REFERENCE 6

AUTHORS RIKEN Genome Exploration Research Group, Genome Science Group (Genome Network Core Team) and the FANTOM Consortium.

TITLE Antisense Transcription in the Mammalian Transcriptome

JOURNAL Science 309, 1564-1566 (2005)

REFERENCE 7

AUTHORS The FANTOM Consortium, Riken Genome Exploration Research Group and Genome Science Group (Genome Network Project Core Group).

TITLE The Transcriptional Landscape of the Mammalian Genome

JOURNAL Science 309, 1559-1563 (2005)

REFERENCE 8 (bases 1 to 3185)

AUTHORS Adachi, J., Aizawa, K., Akimura, T., Arakawa, T., Bono, H., Carninci, P., Fukuda, S., Furuno, M., Hanagaki, T., Hara, A., Hashizume, W., Hayashida, K., Hayatsu, N., Hiramoto, K., Hiraoka, T., Hirozane, T., Hori, F., Imotani, K., Ishii, Y., Itoh, M., Kagawa, I., Kasukawa, T., Katoh, H., Kawai, J., Kojima, Y., Kondo, S., Konno, H., Kouda, M., Koya, S., Kurihara, C., Matsuyama, T., Miyazaki, A., Murata, M., Nakamura, M., Nishi, K., Nomura, K., Numazaki, R., Ohno, M., Ohsato, N.,

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Okazaki,Y., Saito,R., Saitoh,H., Sakai,C., Sakai,K., Sakazume,N., Sano,H., Sasaki,D., Shibata,K., Shinagawa,A., Shiraki,T., Sogabe,Y., Tagami,M., Tagawa,A., Takahashi,F., Takaku-Akahira,S., Takeda,Y., Tanaka,T., Tomaru,A., Toya,T., Yasunishi,A., Muramatsu,M. and Hayashizaki,Y.

TITLE Direct Submission

JOURNAL Submitted (16-JUL-2001) Yoshihide Hayashizaki, The Institute of Physical and Chemical Research (RIKEN), Laboratory for Genome Exploration Research Group, RIKEN Genomic Sciences Center (GSC), RIKEN Yokohama Institute; 1-7-22 Suehiro-cho, Tsurumi-ku, Yokohama, Kanagawa, 230-0045, Japan (E-mail:genome-res@gsc.riken.jp, URL:http://genome.gsc.riken.jp/, Tel:81-45-503-9222, Fax:81-45-503-9216)

COMMENT cDNA library was prepared and sequenced in Mouse Genome Encyclopedia Project of Genome Exploration Research Group in Riken Genomic Sciences Center and Genome Science Laboratory in RIKEN. Division of Experimental Animal Research in Riken contributed to prepare mouse tissues. Please visit our web site for further details. URL:http://genome.gsc.riken.jp/ URL:http://fantom.gsc.riken.jp/.

FEATURES Location/Qualifiers

source 1. .3185
 /organism="Mus musculus"
 /mol_type="mRNA"
 /strain="C57BL/6J"
 /db_xref="FANTOM_DB:A830043F14"
 /db_xref="taxon:10090"
 /clone="A830043F14"
 /tissue_type="cortex"
 /clone_lib="RIKEN full-length enriched mouse cDNA library"
 /dev_stage="10 days neonate"

CDS 389. .2233
 /note="unnamed protein product; HYPOTHETICAL 71.0 KDA PROTEIN homolog [Mus musculus] (SPTR|AAH21749, evidence: FASTY, 99.8%ID, 100%length, match=1842) putative"
 /codon_start=1
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 /db_xref="GI:26335972"
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polyA_signal 3168. .3173
 /note="putative"

polyA_site 3185
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ORIGIN

Query Match 99.4%; Score 2676; DB 6; Length 3185;
 Best Local Similarity 99.9%; Pred. No. 0;
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Qy 1 CGTAGGAGAGTGACAGGAGCTGTTGTAAGCGTCGACACTGAGCCGCTCTCAGGTAT 60

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Db      310  |||||CGTAGGAGAGTGACAGGAGCTGTTGTAAGCGTCGCAGCACTGAGCCGCCTCCTCAGGTAT 369
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Db      370  |||||CCTGGCTCTGGAACCTTGCTATGGGAGATTGGATGACTGTGACAGATCCAGTTCTGTGTAC 429
Qy      121  AGAAAACAAAATCTCTCTCAATATACCTCAGAAAACAAAGATGTCTCCGTCCAGTTTGTGA 180
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Qy      181  CTCCCAGCAAGTTCTGTGCTCTTCAGTACCTTTATCCAAAACGTGCATGGTGTTCG 240
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Qy      241  TGTCTTCTGCACAGGAGAGAACATTGAACAAAGTATTTCTATCTTGATCAGGAGCTGAC 300
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Db      790  |||||GCAGAGCTGCTACGCCAACTTAAGGAGCAGTTGGAAACGTCCAGGCGGGAGATGATCGG 849
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Qy      601  GAATGAGAAAGATGAGGTACAAAAATTACAAAATATCATAGCCAGCCGGGCTACTCAGTA 660
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Db      1210 |||||CGCGGAGCTGAAGAAGGTCTCCAGCAGATGAAGAAGGAGATGATCTCTCTCTGTCTCC 1269

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Qy	1081	TGTGAGAGAGCAGCTGACAAAACAGCATCAGGAAACAGTGGAGAATTTTGAAAAGTCATGT	1140
Db	1390	TGTGAGAGAGCAGCTGACAAAACAGCATCAGGAAACAGTGGAGAATTTTGAAAAGTCATGT	1449
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Qy	1201	CATCTCACGACAAGACCATGAGCAAGAGACTGAGAAACTGGAGCTGGAGATTGAGCGGTG	1260
Db	1510	CATCTCACGACAAGACCATGAGCAAGAGACTGAGAAACTGGAGCTGGAGATTGAGCGGTG	1569
Qy	1261	TAAAGAGATGATCAAGGCTCAGCAGCAGCTCTTACAGCAGCAGCTGGCCACCACGTGTGA	1320
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Qy	1381	AGAAGAGTGGACCCTTTTTAAAGAGCAAAAAAGAATTTTGAGAGAGAAAGGCGAAGCTT	1440
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Qy	1501	CTGGGTAAAGCAGCAGTTTTTAAACATGACGAACTTTGACCACCAGAACTCAGAAAATGT	1560
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Qy	1561	GAACTTTTCAGTGCCTTCTCAGGAAGTCTGATCCAGACAATCTTATAGTCCACTCACG	1620
Db	1867	GAACTTTTCAGTGCCTTCTCAGGAAGTCTGATCCAGACAATCTTATAGTCCACTCACG	1926
Qy	1621	GCCACGGCAAAAGAAGCTACACAGTGTGGCTAATGGGGTGCCAGCTTGACATCAAACT	1680
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Qy	1681	GACTAAATCTCTTCCTGCCTCACCTTCTACTTCAGACTTTGCGCAGACACATTATGTGT	1740
Db	1987	GACTAAATCTCTTCCTGCCTCACCTTCTACTTCAGACTTTGCGCAGACACATTATGTGT	2046
Qy	1741	GTCTGAACACAGTTCATCAGTGTGCTGAATATAACTCCTGAAGAAAGTAAACCAAGTGA	1800
Db	2047	GTCTGAACACAGTTCATCAGTGTGCTGAATATAACTCCTGAAGAAAGTAAACCAAGTGA	2106
Qy	1801	GGTTGCAAGAGAAAGCACGGATCAGAAGTGGAGCGTGCAGTCGAGGCCAGCTCGCGGGA	1860
Db	2107	GGTTGCAAGAGAAAGCACGGATCAGAAGTGGAGCGTGCAGTCGAGGCCAGCTCGCGGGA	2166
Qy	1861	GGGGTGCTACAGCGGATGCTCCTCGGCCTTCAGGAGCGCTCAGGGGACCGAGATGACTT	1920

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Db 2167 ||||| GGGGTGCTACAGCGGATGCTCCTCGGCCTTCAGGAGCGCTCACGGGGACCGAGATGACTT 2226

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Db 2347 TGTCTTCCCCCAAAGAGCTGAAATGCTAAGCTACTTAAAAGGATGCAAAGCTTTGGTTGT 2406

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Db 2887 ATAAGTAGAAGTAACTAAGTACATTTTGTAGATTTTAAAGCATTGTATTTTATTTTAT 2946

Qy 2641 ATATGTGAATGTTATAATTTCTAAGAGGAATATTGATTATGGAGTAATGGGG 2692

Db 2947 ATATGTGAATGTTATAATTTCTAAGAGGAATATTGATTATGGAGTAATGGGG 2998

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12. Claims 1,3, 4, 6, 15-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Carninci et. al. (Genome Research, Vol. 10, pages 1617-1630, 2000)

Carninci et. al. (also see attached sequence comparison) disclose a polynucleotide, which has 99.4% query match and 99.9% identity to the polynucleotide of SEQ ID NO:1. Also disclosed are vector comprising said polynucleotide and cell comprising said vector. The disclosed polynucleotide encodes a polypeptide that inherently binds afadin and/or actinin, absent evidence to the contrary.

Therefore the disclosure of Carninci et. al. meets the limitations of claims 1,3, 4, 6, 15-18, absent evidence to the contrary.

RESULT 1
AK043865
LOCUS AK043865 3185 bp mRNA linear HTC 02-SEP-2005
DEFINITION Mus musculus 10 days neonate cortex cDNA, RIKEN full-length enriched library, clone:A830043F14 product:HYPOTHETICAL 71.0 KDA PROTEIN homolog [Mus musculus], full insert sequence.
ACCESSION AK043865
VERSION AK043865.1 GI:26335971
KEYWORDS HTC; CAP trapper.
SOURCE Mus musculus (house mouse)
ORGANISM Mus musculus
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Sciurognathi; Muroidea; Muridae; Murinae; Mus.
REFERENCE 1
AUTHORS Carninci,P. and Hayashizaki,Y.
TITLE High-efficiency full-length cDNA cloning
JOURNAL Meth. Enzymol. 303, 19-44 (1999)
PUBMED 10349636
REFERENCE 2
AUTHORS Carninci,P., Shibata,Y., Hayatsu,N., Sugahara,Y., Shibata,K., Itoh,M., Konno,H., Okazaki,Y., Muramatsu,M. and Hayashizaki,Y.
TITLE Normalization and subtraction of cap-trapper-selected cDNAs to prepare full-length cDNA libraries for rapid discovery of new genes
JOURNAL Genome Res. 10 (10), 1617-1630 (2000)
PUBMED 11042159
REFERENCE 3
AUTHORS Shibata,K., Itoh,M., Aizawa,K., Nagaoka,S., Sasaki,N., Carninci,P., Konno,H., Akiyama,J., Nishi,K., Kitsunai,T., Tashiro,H., Itoh,M., Sumi,N., Ishii,Y., Nakamura,S., Hazama,M., Nishine,T., Harada,A., Yamamoto,R., Matsumoto,H., Sakaguchi,S., Ikegami,T., Kashiwagi,K., Fujiwake,S., Inoue,K., Togawa,Y., Izawa,M., Ohara,E., Watahiki,M.,

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Yoneda,Y., Ishikawa,T., Ozawa,K., Tanaka,T., Matsuura,S., Kawai,J., Okazaki,Y., Muramatsu,M., Inoue,Y., Kira,A. and Hayashizaki,Y.

TITLE RIKEN integrated sequence analysis (RISA) system--384-format sequencing pipeline with 384 multicapillary sequencer

JOURNAL Genome Res. 10 (11), 1757-1771 (2000)

PUBMED 11076861

REFERENCE 4

AUTHORS The RIKEN Genome Exploration Research Group Phase II Team and the FANTOM Consortium.

TITLE Functional annotation of a full-length mouse cDNA collection

JOURNAL Nature 409, 685-690 (2001)

REFERENCE 5

AUTHORS The FANTOM Consortium, the RIKEN Genome Exploration Research Group Phase I and II Team.

TITLE Analysis of the mouse transcriptome based on functional annotation of 60,770 full-length cDNAs

JOURNAL Nature 420, 563-573 (2002)

REFERENCE 6

AUTHORS RIKEN Genome Exploration Research Group, Genome Science Group (Genome Network Core Team) and the FANTOM Consortium.

TITLE Antisense Transcription in the Mammalian Transcriptome

JOURNAL Science 309, 1564-1566 (2005)

REFERENCE 7

AUTHORS The FANTOM Consortium, Riken Genome Exploration Research Group and Genome Science Group (Genome Network Project Core Group).

TITLE The Transcriptional Landscape of the Mammalian Genome

JOURNAL Science 309, 1559-1563 (2005)

REFERENCE 8 (bases 1 to 3185)

AUTHORS Adachi,J., Aizawa,K., Akimura,T., Arakawa,T., Bono,H., Carninci,P., Fukuda,S., Furuno,M., Hanagaki,T., Hara,A., Hashizume,W., Hayashida,K., Hayatsu,N., Hiramoto,K., Hiraoka,T., Hirozane,T., Hori,F., Imotani,K., Ishii,Y., Itoh,M., Kagawa,I., Kasukawa,T., Katoh,H., Kawai,J., Kojima,Y., Kondo,S., Konno,H., Kouda,M., Koya,S., Kurihara,C., Matsuyama,T., Miyazaki,A., Murata,M., Nakamura,M., Nishi,K., Nomura,K., Numazaki,R., Ohno,M., Ohsato,N., Okazaki,Y., Saito,R., Saitoh,H., Sakai,C., Sakai,K., Sakazume,N., Sano,H., Sasaki,D., Shibata,K., Shinagawa,A., Shiraki,T., Sogabe,Y., Tagami,M., Tagawa,A., Takahashi,F., Takaku-Akahira,S., Takeda,Y., Tanaka,T., Tomaru,A., Toya,T., Yasunishi,A., Muramatsu,M. and Hayashizaki,Y.

TITLE Direct Submission

JOURNAL Submitted (16-JUL-2001) Yoshihide Hayashizaki, The Institute of Physical and Chemical Research (RIKEN), Laboratory for Genome Exploration Research Group, RIKEN Genomic Sciences Center (GSC), RIKEN Yokohama Institute; 1-7-22 Suehiro-cho, Tsurumi-ku, Yokohama, Kanagawa, 230-0045, Japan (E-mail:genome-res@gsc.riken.jp, URL:http://genome.gsc.riken.jp/, Tel:81-45-503-9222, Fax:81-45-503-9216)

COMMENT cDNA library was prepared and sequenced in Mouse Genome Encyclopedia Project of Genome Exploration Research Group in Riken Genomic Sciences Center and Genome Science Laboratory in RIKEN. Division of Experimental Animal Research in Riken contributed to prepare mouse tissues. Please visit our web site for further details. URL:http://genome.gsc.riken.jp/ URL:http://fantom.gsc.riken.jp/.

FEATURES Location/Qualifiers

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/mol_type="mRNA"
/strain="C57BL/6J"
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ORIGIN

Query Match 99.4%; Score 2676; DB 6; Length 3185;
Best Local Similarity 99.9%; Pred. No. 0;
Matches 2689; Conservative 0; Mismatches 0; Indels 3; Gaps 1;

Qy	1	CGTAGGAGAGTGACAGGAGCTGTTGTAAGCGTCGCAGCACTGAGCCGCCTCCTCAGGTAT	60
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Qy	2641	ATATGTGAATGTTATAATTTCTAAGAGGAATATTGATTATGGAGTAATGGGG	2692
Db	2947	ATATGTGAATGTTATAATTTCTAAGAGGAATATTGATTATGGAGTAATGGGG	2998

14. Claims 1,3, 4, 6, 14-18 are rejected under 35 U.S.C. 102(a) as being anticipated by Mammalian Gene Collection (MGC) Program team (PNAS, Vol. 99, pages 16899-16903), December 24, 2002)

MGC Program team (also see attached sequence comparison) disclose a polynucleotide, which has 99.9% query match and 99.9% identity to the polynucleotide of SEQ ID NO:1. MGC Program team also disclose the polynucleotide encodes a polypeptide that has 100% query match and 100% identity to the polypeptide of SEQ ID NO:2. The disclosed polynucleotide encodes a polypeptide that inherently binds afadin and/or actinin, absent evidence to the contrary.

Further disclosed is vector comprising said polynucleotide and cell comprising said vector. Therefore the disclosure of the MGC Program meets the

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limitations of claims 1,3, 4, 6, 14-18, absent evidence to the contrary.

RESULT 3

BC021749

LOCUS BC021749 3425 bp mRNA linear ROD 18-JUL-2005

DEFINITION Mus musculus synovial sarcoma, X breakpoint 2 interacting protein, mRNA (cDNA clone MGC:25823 IMAGE:4165430), complete cds.

ACCESSION BC021749

VERSION BC021749.1 GI:18256805

KEYWORDS MGC.

SOURCE Mus musculus (house mouse)

ORGANISM Mus musculus

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Sciurognathi; Muroidea; Muridae; Murinae; Mus.

REFERENCE 1 (bases 1 to 3425)

AUTHORS

Strausberg,R.L., Feingold,E.A., Grouse,L.H., Derge,J.G., Klausner,R.D., Collins,F.S., Wagner,L., Shenmen,C.M., Schuler,G.D., Altschul,S.F., Zeeberg,B., Buetow,K.H., Schaefer,C.F., Bhat,N.K., Hopkins,R.F., Jordan,H., Moore,T., Max,S.I., Wang,J., Hsieh,F., Diatchenko,L., Marusina,K., Farmer,A.A., Rubin,G.M., Hong,L., Stapleton,M., Soares,M.B., Bonaldo,M.F., Casavant,T.L., Scheetz,T.E., Brownstein,M.J., Usdin,T.B., Toshiyuki,S., Carninci,P., Prange,C., Raha,S.S., Loquellano,N.A., Peters,G.J., Abramson,R.D., Mullahy,S.J., Bosak,S.A., McEwan,P.J., McKernan,K.J., Malek,J.A., Gunaratne,P.H., Richards,S., Worley,K.C., Hale,S., Garcia,A.M., Gay,L.J., Hulyk,S.W., Villalon,D.K., Muzny,D.M., Sodergren,E.J., Lu,X., Gibbs,R.A., Fahey,J., Helton,E., Kettelman,M., Madan,A., Rodrigues,S., Sanchez,A., Whiting,M., Madan,A., Young,A.C., Shevchenko,Y., Bouffard,G.G., Blakesley,R.W., Touchman,J.W., Green,E.D., Dickson,M.C., Rodriguez,A.C., Grimwood,J., Schmutz,J., Myers,R.M., Butterfield,Y.S., Krzywinski,M.I., Skalska,U., Smailus,D.E., Schnerch,A., Schein,J.E., Jones,S.J. and Marra,M.A.

CONSRTM Mammalian Gene Collection Program Team

TITLE Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences

JOURNAL Proc. Natl. Acad. Sci. U.S.A. 99 (26), 16899-16903 (2002)

PUBMED 12477932

REFERENCE 2 (bases 1 to 3425)

AUTHORS

CONSRTM NIH MGC Project

TITLE Direct Submission

JOURNAL Submitted (18-JAN-2002) National Institutes of Health, Mammalian Gene Collection (MGC), Bethesda, MD 20892-2590, USA

REMARK NIH-MGC Project URL: <http://mgc.nci.nih.gov>

COMMENT Contact: MGC help desk

Email: cgapbs-r@mail.nih.gov

Tissue Procurement: Jeffrey E. Green, M.D.

cDNA Library Preparation: Life Technologies, Inc.

cDNA Library Arrayed by: The I.M.A.G.E. Consortium (LLNL)

DNA Sequencing by: Baylor College of Medicine Human Genome Sequencing Center

Center code: BCM-HGSC

Web site: <http://www.hgsc.bcm.tmc.edu/cdna/>Contact: amg@bcm.tmc.edu

Gunaratne, P.H., Garcia, A.M., Lu, X., Hulyk, S.W., Loulseged, H., Kowis, C.R., Sneed, A.J., Martin, R.G., Muzny, D.M., Nanavati, A.N., Gibbs, R.A.

Clone distribution: MGC clone distribution information can be found

through the I.M.A.G.E. Consortium/LLNL at: <http://image.llnl.gov>
Series: IRAK Plate: 30 Row: m Column: 16.

FEATURES	Location/Qualifiers
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ORIGIN

Query Match 99.9%; Score 2688.8; DB 6; Length 3425;
Best Local Similarity 99.9%; Pred. No. 0;
Matches 2690; Conservative 0; Mismatches 2; Indels 0; Gaps 0;

[illegible]

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```

15. No claim is allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**.

See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory

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period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Advisory

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NCB
Nirmal S. Basi
Art Unit 1646

Gary Nickol

GARY B. NICKOL, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Appendix 1



IFW16

RAW SEQUENCE LISTING

DATE: 12/28/2006

PATENT APPLICATION: US/10/644,084A

TIME: 18:31:08

Input Set : A:\2144.0100000_E1-X0202-USsq.txt

Output Set: N:\CRF4\12282006\J644084A.raw

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5 <120> TITLE OF INVENTION: ADIP PROTEIN AND USE THEREOF
7 <130> FILE REFERENCE: 2144.0100000
9 <140> CURRENT APPLICATION NUMBER: US 10/644,084A
10 <141> CURRENT FILING DATE: 2003-08-20
12 <150> PRIOR APPLICATION NUMBER: JP 2002-284263
13 <151> PRIOR FILING DATE: 2002-09-27
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62 Val Leu Gln Arg Lys Asn Leu Leu Ala Gln Glu Ser Val Glu Thr Gln
63 110 115 120

see p. 6

RAW SEQUENCE LISTING

DATE: 12/28/2006

PATENT APPLICATION: US/10/644,084A

TIME: 18:31:08

Input Set : A:\2144.0100000_E1-X0202-USsq.txt

Output Set: N:\CRF4\12282006\J644084A.raw

65	aac	ttg	aag	ctg	ggc	agt	gac	atg	gac	cac	ctg	cag	agc	tgc	tac	gcc	496
66	Asn	Leu	Lys	Leu	Gly	Ser	Asp	Met	Asp	His	Leu	Gln	Ser	Cys	Tyr	Ala	
67	125						130				135						
69	aaa	ctt	aag	gag	cag	ttg	gaa	acg	tcc	agg	cgg	gag	atg	atc	ggg	ctt	544
70	Lys	Leu	Lys	Glu	Gln	Leu	Glu	Thr	Ser	Arg	Arg	Glu	Met	Ile	Gly	Leu	
71	140					145					150					155	
73	caa	gag	aga	gac	agg	cag	ctg	cag	tgc	aag	aac	agg	agt	ttg	cat	cag	592
74	Gln	Glu	Arg	Asp	Arg	Gln	Leu	Gln	Cys	Lys	Asn	Arg	Ser	Leu	His	Gln	
75					160						165					170	
77	ctc	ctg	aag	aat	gag	aaa	gat	gag	gta	caa	aaa	tta	caa	aat	atc	ata	640
78	Leu	Leu	Lys	Asn	Glu	Lys	Asp	Glu	Val	Gln	Lys	Leu	Gln	Asn	Ile	Ile	
79			175						180						185		
81	gcc	agc	cgg	gct	act	cag	tat	aat	cat	gat	gtg	aag	agg	aag	gag	cgt	688
82	Ala	Ser	Arg	Ala	Thr	Gln	Tyr	Asn	His	Asp	Val	Lys	Arg	Lys	Glu	Arg	
83			190						195						200		
85	gaa	tat	aat	aag	cta	aag	gag	cgc	ctg	cat	cag	ctc	ggt	atg	aac	aag	736
86	Glu	Tyr	Asn	Lys	Leu	Lys	Glu	Arg	Leu	His	Gln	Leu	Val	Met	Asn	Lys	
87		205					210					215					
89	aag	gat	aaa	aac	ata	gcc	atg	gat	gtt	tta	aat	tat	gtg	ggt	cga	gct	784
90	Lys	Asp	Lys	Asn	Ile	Ala	Met	Asp	Val	Leu	Asn	Tyr	Val	Gly	Arg	Ala	
91	220					225					230					235	
93	gat	ggc	aaa	cga	ggc	tca	tgg	agg	act	gac	aaa	aca	gaa	gcc	agg	aat	832
94	Asp	Gly	Lys	Arg	Gly	Ser	Trp	Arg	Thr	Asp	Lys	Thr	Glu	Ala	Arg	Asn	
95				240						245					250		
97	gaa	gat	gag	atg	tac	aaa	att	ctg	ttg	aat	gat	tat	gag	tac	cgc	cag	880
98	Glu	Asp	Glu	Met	Tyr	Lys	Ile	Leu	Leu	Asn	Asp	Tyr	Glu	Tyr	Arg	Gln	
99			255						260						265		
101	aag	cag	atc	ctg	atg	gag	aac	gcg	gag	ctg	aag	aag	gtc	ctc	cag	cag	928
102	Lys	Gln	Ile	Leu	Met	Glu	Asn	Ala	Glu	Leu	Lys	Lys	Val	Leu	Gln	Gln	
103			270					275					280				
105	atg	aag	aag	gag	atg	atc	tct	ctc	ctg	tct	cct	cag	aag	aag	aag	ccc	976
106	Met	Lys	Lys	Glu	Met	Ile	Ser	Leu	Leu	Ser	Pro	Gln	Lys	Lys	Lys	Pro	
107			285					290					295				
109	agg	gaa	aga	gca	gag	gac	ggc	aca	ggc	act	gtt	gct	atc	tcc	gat	ata	1024
110	Arg	Glu	Arg	Ala	Glu	Asp	Gly	Thr	Gly	Thr	Val	Ala	Ile	Ser	Asp	Ile	
111	300					305					310					315	
113	gaa	gat	gac	tct	ggg	gaa	ctg	agc	aga	gac	agc	gtg	tgg	ggc	ctt	tcc	1072
114	Glu	Asp	Asp	Ser	Gly	Glu	Leu	Ser	Arg	Asp	Ser	Val	Trp	Gly	Leu	Ser	
115				320						325					330		
117	tgt	gac	act	gtg	aga	gag	cag	ctg	aca	aac	agc	atc	agg	aaa	cag	tgg	1120
118	Cys	Asp	Thr	Val	Arg	Glu	Gln	Leu	Thr	Asn	Ser	Ile	Arg	Lys	Gln	Trp	
119				335					340						345		
121	aga	att	ttg	aaa	agt	cat	gta	gaa	aaa	ctc	gat	aac	caa	gct	tcg	aag	1168
122	Arg	Ile	Leu	Lys	Ser	His	Val	Glu	Lys	Leu	Asp	Asn	Gln	Ala	Ser	Lys	
123			350						355						360		
125	gta	cac	tca	gag	ggc	ctt	aat	gag	gag	gac	gtc	atc	tca	cga	caa	gac	1216
126	Val	His	Ser	Glu	Gly	Leu	Asn	Glu	Glu	Asp	Val	Ile	Ser	Arg	Gln	Asp	
127		365					370					375					
129	cat	gag	caa	gag	act	gag	aaa	ctg	gag	ctg	gag	att	gag	cgg	tgt	aaa	1264

RAW SEQUENCE LISTING

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Input Set : A:\2144.0100000_E1-X0202-USsq.txt

Output Set: N:\CRF4\12282006\J644084A.raw

130	His	Glu	Gln	Glu	Thr	Glu	Lys	Leu	Glu	Leu	Glu	Ile	Glu	Arg	Cys	Lys	
131	380					385					390					395	
133	gag	atg	atc	aag	gct	cag	cag	cag	ctc	tta	cag	cag	cag	ctg	gcc	acc	1312
134	Glu	Met	Ile	Lys	Ala	Gln	Gln	Gln	Leu	Leu	Gln	Gln	Gln	Leu	Ala	Thr	
135					400					405					410		
137	acg	tgt	gat	gat	gac	acc	acc	tca	ctg	ttg	cga	gac	tgt	tac	ttg	ctg	1360
138	Thr	Cys	Asp	Asp	Asp	Thr	Thr	Ser	Leu	Leu	Arg	Asp	Cys	Tyr	Leu	Leu	
139					415					420					425		
141	gaa	gaa	aag	gaa	cgc	ctt	aaa	gaa	gag	tggt	acc	ctt	ttt	aaa	gag	caa	1408
142	Glu	Glu	Lys	Glu	Arg	Leu	Lys	Glu	Trp	Thr	Leu	Phe	Lys	Glu	Gln		
143					430				435					440			
145	aaa	aag	aat	ttt	gag	aga	gaa	agg	cga	agc	ttt	aca	gaa	gct	gcc	att	1456
146	Lys	Lys	Asn	Phe	Glu	Arg	Glu	Arg	Arg	Ser	Phe	Thr	Glu	Ala	Ala	Ile	
147		445					450					455					
149	cga	ttg	ggg	ttg	gag	aga	aag	gag	ttt	gaa	gaa	gag	cga	gcc	agc	tggt	1504
150	Arg	Leu	Gly	Leu	Glu	Arg	Lys	Ala	Phe	Glu	Glu	Glu	Arg	Ala	Ser	Trp	
151	460					465				470					475		
153	gta	aag	cag	cag	ttt	tta	aac	atg	acg	aac	ttt	gac	cac	cag	aac	tca	1552
154	Val	Lys	Gln	Gln	Phe	Leu	Asn	Met	Thr	Asn	Phe	Asp	His	Gln	Asn	Ser	
155					480					485					490		
157	gaa	aat	gtg	aaa	ctt	ttc	agt	gcc	ttc	tca	gga	agt	tct	gat	cca	gac	1600
158	Glu	Asn	Val	Lys	Leu	Phe	Ser	Ala	Phe	Ser	Gly	Ser	Ser	Asp	Pro	Asp	
159					495				500					505			
161	aat	ctt	ata	gtc	cac	tca	cgg	cca	cgg	caa	aag	aag	cta	cac	agt	gtg	1648
162	Asn	Leu	Ile	Val	His	Ser	Arg	Pro	Arg	Gln	Lys	Lys	Leu	His	Ser	Val	
163			510					515					520				
165	gct	aat	ggg	gtg	cca	gct	tgc	aca	tca	aaa	ctg	act	aaa	tct	ctt	cct	1696
166	Ala	Asn	Gly	Val	Pro	Ala	Cys	Thr	Ser	Lys	Leu	Thr	Lys	Ser	Leu	Pro	
167		525					530					535					
169	gcc	tca	cct	tct	act	tca	gac	ttt	cgc	cag	aca	cat	tca	tgt	gtg	tct	1744
170	Ala	Ser	Pro	Ser	Thr	Ser	Asp	Phe	Arg	Gln	Thr	His	Ser	Cys	Val	Ser	
171	540					545				550					555		
173	gaa	cac	agt	tcc	atc	agt	gtg	ctg	aat	ata	act	cct	gaa	gaa	agt	aaa	1792
174	Glu	His	Ser	Ser	Ile	Ser	Val	Leu	Asn	Ile	Thr	Pro	Glu	Glu	Ser	Lys	
175					560				565					570			
177	cca	agt	gag	gtt	gca	aga	gaa	agc	acg	gat	cag	aag	tggt	agc	gtg	cag	1840
178	Pro	Ser	Glu	Val	Ala	Arg	Glu	Ser	Thr	Asp	Gln	Lys	Trp	Ser	Val	Gln	
179					575				580					585			
181	tcg	agg	ccc	agc	tcg	cgg	gag	ggg	tgc	tac	agc	gga	tgc	tcc	tcg	gcc	1888
182	Ser	Arg	Pro	Ser	Ser	Arg	Glu	Gly	Cys	Tyr	Ser	Gly	Cys	Ser	Ser	Ala	
183			590					595					600				
185	ttc	agg	agc	gct	cac	ggg	gac	cga	gat	gac	tta	cct	taa	atgtgcgggc			1937
186	Phe	Arg	Ser	Ala	His	Gly	Asp	Arg	Asp	Asp	Leu	Pro					
187		605				610					615						
189	tgca	gtgctg	ttcccagatg	tgcgctagag	gagttgacac	agggtgtagc	ataaaagtcag										1997
191	tcgtctaact	taagatgctc	agagttgttt	gtttggactt	cgctgtcttc	ccccaaagag											2057
193	ctgaaatgct	aagctactta	aaaggatgca	aagctttggg	tgtgtgttag	taacagaagc											2117
195	ccctggctct	gtgactgcag	gaatgcatgg	cgtttggatg	gaaacagaag	cgctggaatg											2177
197	attgcctcgc	caggtaccga	gaagagcact	tttagggact	ggttcctgta	aacattaaat											2237

RAW SEQUENCE LISTING

DATE: 12/28/2006

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TIME: 18:31:08

Input Set : A:\2144.0100000_E1-X0202-USsq.txt

Output Set: N:\CRF4\12282006\J644084A.raw

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199 attcggtccca agtgtggttg gcattggaag tgtagccttt acttgaatgt atactgtaga 2297
201 tttttaacaa agcagggttct atatttatta tgtttagtgt gattttggga ttacctcttt 2357
203 catatgtttt gtgtctgtac ataaatatac atgactatgt taagaggctt taaggtttaa 2417
205 aaacttcaca ccatgcttga gtatagcatt tcatgccaat taaaatgttt tcagtggcat 2477
207 ggtgtttaca gaggttagga cactgccac atgacagtta agactttatt ttttagccat 2537
209 ctgggcaata aaaattcaaa gccccttcat aagctgagtt cagataacta gaactactaa 2597
211 cgttacattt ttgagatttt taaagcattg tattttattt tatatatgtg aatgttataa 2657
213 tttctaagag gaattattgat tatggagtaa tggggg 2692
216 <210> SEQ ID NO: 2
217 <211> LENGTH: 615
218 <212> TYPE: PRT
219 <213> ORGANISM: Mus musculus
221 <400> SEQUENCE: 2
223 Met Gly Asp Trp Met Thr Val Thr Asp Pro Val Leu Cys Thr Glu Asn
224 1 5 10 15
227 Lys Asn Leu Ser Gln Tyr Thr Ser Glu Thr Lys Met Ser Pro Ser Ser
228 20 25 30
231 Leu Tyr Ser Gln Gln Val Leu Cys Ser Ser Val Pro Leu Ser Lys Asn
232 35 40 45
235 Val His Gly Val Phe Gly Val Phe Cys Thr Gly Glu Asn Ile Glu Gln
236 50 55 60
239 Ser Ile Ser Tyr Leu Asp Gln Glu Leu Thr Thr Phe Gly Phe Pro Ser
240 65 70 75 80
243 Leu Tyr Glu Glu Ser Lys Ser Lys Glu Ala Lys Arg Glu Leu Asn Ile
244 85 90 95
247 Val Ala Val Leu Asn Cys Met Asn Glu Leu Leu Val Leu Gln Arg Lys
248 100 105 110
251 Asn Leu Leu Ala Gln Glu Ser Val Glu Thr Gln Asn Leu Lys Leu Gly
252 115 120 125
255 Ser Asp Met Asp His Leu Gln Ser Cys Tyr Ala Lys Leu Lys Glu Gln
256 130 135 140
259 Leu Glu Thr Ser Arg Arg Glu Met Ile Gly Leu Gln Glu Arg Asp Arg
260 145 150 155 160
263 Gln Leu Gln Cys Lys Asn Arg Ser Leu His Gln Leu Leu Lys Asn Glu
264 165 170 175
267 Lys Asp Glu Val Gln Lys Leu Gln Asn Ile Ile Ala Ser Arg Ala Thr
268 180 185 190
271 Gln Tyr Asn His Asp Val Lys Arg Lys Glu Arg Glu Tyr Asn Lys Leu
272 195 200 205
275 Lys Glu Arg Leu His Gln Leu Val Met Asn Lys Lys Asp Lys Asn Ile
276 210 215 220
279 Ala Met Asp Val Leu Asn Tyr Val Gly Arg Ala Asp Gly Lys Arg Gly
280 225 230 235 240
283 Ser Trp Arg Thr Asp Lys Thr Glu Ala Arg Asn Glu Asp Glu Met Tyr
284 245 250 255
287 Lys Ile Leu Leu Asn Asp Tyr Glu Tyr Arg Gln Lys Gln Ile Leu Met
288 260 265 270
291 Glu Asn Ala Glu Leu Lys Lys Val Leu Gln Gln Met Lys Lys Glu Met
292 275 280 285

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RAW SEQUENCE LISTING

DATE: 12/28/2006

PATENT APPLICATION: US/10/644,084A

TIME: 18:31:08

Input Set : A:\2144.0100000_E1-X0202-USsq.txt

Output Set: N:\CRF4\12282006\J644084A.raw

```

295 Ile Ser Leu Leu Ser Pro Gln Lys Lys Lys Pro Arg Glu Arg Ala Glu
296      290      295      300
299 Asp Gly Thr Gly Thr Val Ala Ile Ser Asp Ile Glu Asp Asp Ser Gly
300 305      310      315      320
303 Glu Leu Ser Arg Asp Ser Val Trp Gly Leu Ser Cys Asp Thr Val Arg
304      325      330      335
307 Glu Gln Leu Thr Asn Ser Ile Arg Lys Gln Trp Arg Ile Leu Lys Ser
308      340      345      350
311 His Val Glu Lys Leu Asp Asn Gln Ala Ser Lys Val His Ser Glu Gly
312      355      360      365
315 Leu Asn Glu Glu Asp Val Ile Ser Arg Gln Asp His Glu Gln Glu Thr
316      370      375      380
319 Glu Lys Leu Glu Leu Glu Ile Glu Arg Cys Lys Glu Met Ile Lys Ala
320 385      390      395      400
323 Gln Gln Gln Leu Leu Gln Gln Gln Leu Ala Thr Thr Cys Asp Asp Asp
324      405      410      415
327 Thr Thr Ser Leu Leu Arg Asp Cys Tyr Leu Leu Glu Glu Lys Glu Arg
328      420      425      430
331 Leu Lys Glu Glu Trp Thr Leu Phe Lys Glu Gln Lys Lys Asn Phe Glu
332      435      440      445
335 Arg Glu Arg Arg Ser Phe Thr Glu Ala Ala Ile Arg Leu Gly Leu Glu
336      450      455      460
339 Arg Lys Ala Phe Glu Glu Glu Arg Ala Ser Trp Val Lys Gln Gln Phe
340 465      470      475      480
343 Leu Asn Met Thr Asn Phe Asp His Gln Asn Ser Glu Asn Val Lys Leu
344      485      490      495
347 Phe Ser Ala Phe Ser Gly Ser Ser Asp Pro Asp Asn Leu Ile Val His
348      500      505      510
351 Ser Arg Pro Arg Gln Lys Lys Leu His Ser Val Ala Asn Gly Val Pro
352      515      520      525
355 Ala Cys Thr Ser Lys Leu Thr Lys Ser Leu Pro Ala Ser Pro Ser Thr
356      530      535      540
359 Ser Asp Phe Arg Gln Thr His Ser Cys Val Ser Glu His Ser Ser Ile
360 545      550      555      560
363 Ser Val Leu Asn Ile Thr Pro Glu Glu Ser Lys Pro Ser Glu Val Ala
364      565      570      575
367 Arg Glu Ser Thr Asp Gln Lys Trp Ser Val Gln Ser Arg Pro Ser Ser
368      580      585      590
371 Arg Glu Gly Cys Tyr Ser Gly Cys Ser Ser Ala Phe Arg Ser Ala His
372      595      600      605
375 Gly Asp Arg Asp Asp Leu Pro
376      610      615
379 <210> SEQ ID NO: 3
380 <211> LENGTH: 3195
381 <212> TYPE: DNA
382 <213> ORGANISM: Rattus norvegicus
385 <220> FEATURE:
386 <221> NAME/KEY: CDS
387 <222> LOCATION: (79)..(1920)

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RAW SEQUENCE LISTING ERROR SUMMARY DATE: 12/28/2006
PATENT APPLICATION: US/10/644,084A TIME: 18:31:09

Input Set : A:\2144.0100000_E1-X0202-USsq.txt
Output Set: N:\CRF4\12282006\J644084A.raw

Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220>

to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:3; N Pos. 2422

Invalid <213> Response:

Use of "Artificial" only as "<213> Organism" response is incomplete, per 1.823(b) of New Sequence Rules. Valid response is Artificial Sequence.

Seq#:5,6,7,8

VERIFICATION SUMMARY

DATE: 12/28/2006

PATENT APPLICATION: US/10/644,084A

TIME: 18:31:09

Input Set : A:\2144.0100000_E1-X0202-USsq.txt

Output Set: N:\CRF4\12282006\J644084A.raw

L:569 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:2420